

WHAT IS CLAIMED IS:

1. A method of killing melanoma cells comprising contacting said cells for an effective time with an effective amount of an inhibitor of the MAPK pathway which induces apoptosis in said cells.

2. The method of claim 1, wherein said inhibitor is a MEK-directed protease.

3. The method of claim 2, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

4. The method of claim 1 wherein said inhibitor is an organic small molecule.

5. The method of claim 4 wherein said inhibitor is PD98059, U0126 or PD184352.

6. The method of claim 1, wherein said contacting is *in vivo*.

7. The method of claim 6 wherein said killing results in measurable regression of melanoma tumor or attenuation of melanoma growth.

8. A method of protecting against melanoma in a susceptible subject, comprising administering to said subject that is

- (a) at risk for development of melanoma or,
 - (b) in the case of an already treated subject, at risk for recurrence of melanoma,
- an effective amount of a MAPK-inhibitor.

9. A method of inducing an antitumor response in a mammal having melanoma, comprising administering an effective amount of an inhibitor of the MAPK pathway to said mammal, which inhibitor is cytotoxic to melanoma cells, thereby inducing an antitumor response that is

- (a) a partial antitumor response characterized by
 - (i) at least a 50% decrease in the sum of the products of maximal perpendicular diameters of all measurable lesions;
 - (ii) no evidence of new lesions, and
 - (iii) no progression of any preexisting lesions, or

- (b) a complete antitumor response characterized by the disappearance of all evidence of melanoma disease for at least one month.

10 The method of claim 9 wherein said antitumor response is a partial antitumor response.

5 11. The method of claim 9, wherein said inhibitor is a MEK-directed protease.

12. The method of claim 11, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

13. The method of claim 9 wherein said inhibitor is an organic small molecule.

14 The method of claim 13 wherein said inhibitor is PD98059, U0126 or PD184352.

15 15. The method of any of claims 9-14, wherein said mammal is a human.

16 16. A method of inhibiting growth or recurrent growth of a melanoma tumor in a mammal having melanoma or at risk for melanoma growth or recurrence, comprising administering an effective amount of an inhibitor of the MAPK pathway to said mammal, thereby inducing a cytotoxic response leading to apoptosis of melanoma cells in said mammal, which inhibits said growth or recurrent growth of said melanoma tumor.

17. The method of claim 16 wherein said inhibitor is a MEK-directed protease.

18. The method of claim 17, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

19. The method of claim 16 wherein said inhibitor is an organic small molecule.

20 20 The method of claim 19 wherein said inhibitor is PD98059, U0126 or PD184352.

21. The method of any of claims 16-20, wherein said mammal is a human.

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